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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/057,629	01/25/2002	Harry R. Davis	CV01382K	2175

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PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER	
HUI, SAN MING R	
ART UNIT	**PAPER NUMBER**
1617	

DATE MAILED: 03/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/057,629	DAVIS, HARRY R.	
	Examiner	Art Unit	
	San-ming Hui	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-58* is/are pending in the application.

4a) Of the above claim(s) *2-7,12,25-31,46,47,57 and 58* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,8-11,13-24,32-45 and 48-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 8/21/02, 8/23/02, 1/13/03, 4/14/03, 5/5/03, 5/16/03, 6/9/03
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's response to the restriction requirement of July 2, 2003, submitted August 4, 2003 is acknowledged. Applicant's election with traverse of Group I, claims 1-24, 32-45 and 48-56 and the bile acid sequestrant Cholestyramine, the sterol absorption inhibitor Ezetimibe and a third therapeutic agent, simvastatin, in Paper No. 10 is acknowledged. The traversal is on the ground(s) that it is inappropriate to restrict the invention in the presence of a linking claim. This is not found persuasive because applicant state that there is a linking claim linking the inventions. Note that the restriction requirement is between a product and a process of using the product. Please also note that even if a linking claim were present as contended by the applicant, restriction is appropriate as set forth in MPEP section 809.03.

The requirement is still deemed proper and is therefore made FINAL.

Claims 25-31, 46-47, and 57-58 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed August 4, 2003.

Claims 2-7, and 12 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in response filed August 4, 2003.

Claims 1, 8-11, 13-24, 32-45, and 48-56 have been examined herein to the extent they read on the elected invention and species.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 8-11, 13-24, 32-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In the instant case, the claims are drawn to the prevention of sitosterolemia, a rare genetic disorder that affects the cholesterol storage in the body. The prevention of any genetic disorders is not known in the pharmaceutical field. The only permanent prevention of the genetic disorder will be through genetic manipulation to correct the affected genes. Such genetic manipulation cannot be achieved through administering small molecules compounds to patients. The instant specification does not provide any working examples or guidance as to how such invention work. Absent such guidance and information, one of skilled in the art would have to perform undue experimentation in order to practice the herein claimed invention.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 49-52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 5,767,115. Although the conflicting claims are not identical, they are not patentably distinct from each other because '115 recites the method of preventing atherosclerosis employing the compounds recited in claim 8 of the instant application, which encompass the elected species, ezetimibe (See claim 9).

Claims 49-52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 9 of U.S. Patent No. 5,846,966. Although the conflicting claims are not identical, they are not patentably distinct from each other because '966 recites the method of preventing atherosclerosis employing the compounds recited in claim 8 of the instant application, which encompass the elected species, ezetimibe (See claims 6 and 10).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 48-52 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by '115.

'115 teaches the method of preventing atherosclerosis employing the compounds recited in claim 8 of the instant application, which encompass the elected species, ezetimibe (See claim 9).

Claims 48-52 and 56 are rejected under 35 U.S.C. 102(b) as being anticipated by '966.

'966 teacehs the method of preventing atherosclerosis employing the compounds recited in claim 8 of the instant application, which encompass the elected species, ezetimibe (See claims 6 and 10).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1, 8-9, 10-11, 13-24, 32-42, 53-55 are rejected under 35 U.S.C. 103(a) as being unpatentable over '966 in view of Berge et al. (Secience, 2000; 290:1771-1775).

'966 also teaches the elected compound herein, ezetimibe, with HMG-CoA reductase inhibitors such as simvastatin, useful for reducing cholesterol and the risk of artherosclerosis (See the abstract, also col. 32, Example 6, Compound 6A, and col. 40, line 52 particularly, claims 6 and 10). '966 also teaches the dosage of ezetimibe for treating hypercholesterolemia as0.1-30 or 0.1-15 mg/kg (see col. 21, line 17-19). '966 also teaches the dosage of HMG-CoA reductase inhibitors as 10-80mg daily to 1-1000mg daily depending upon the agents used (See col. 21, lines 27-42).

'966 does not expressly teach the employing of ezetimibe with simvastatin, a HMG-CoA reductase inhibitor, in the dosage herein claimed to treat sitosterolemia.

Berge et al. teaches that hypercholesterolemia is one of the manifestation of sitosterolemia and patients with sitosterolemia are usually hypercholesterolemic (See page 1771 –1772, col. 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ ezetimibe with simvastatin, in the dosage herein claimed to treat sitosterolemia.

One of ordinary skill in the art would have been motivated to employ ezetimibe with simvastatin, in the dosage herein claimed to treat sitosterolemia. '966 teaches the combination of simvastatin and ezetimibe as useful in reducing cholesterol level. Employing the combination of simvastatin and ezetimibe in a method to reduce cholesterol level and thereby treating sitosterolemia would have been reasonably expected to be effective, absent evidence to the contrary. Furthermore, optimization of result effect parameters (e.g., dosage range, dosing regimens) is obvious as being within the skill of the artisan.

Claims 43-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over '966 and Berge et al. as applied to claims 1, 8-9, 10-11, 13-24, 32-42, 53-55 above, and further in view of Hidaka et al. (J. Atheroscler. Thromb., 1995;2(1):60-65).

'966 and Berge et al. suggest the employment of ezetimibe and simvastatin for the treatment of sitosterolemia by reducing the serum cholesterol level.

'966 and Berge et al. do not expressly teach the employment of bile acid sequestrant resin, cholestyramine.

Hidaka et al. teaches that cholestyramine is effective in lowering cholesterol in sitosterolemic patient (See abstract).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate cholestyramine into the method of treating sitasterolemia as suggested by '966 and Berge et al.

One of ordinary skill in the art would have been motivated to incorporate cholestyramine into the method of treating sitasterolemia as suggested by '966 and Berge et al. Since ezetimibe, simvastatin and cholestyramine are known to be useful as cholesterol lowering agent individually, administering all three compounds concomitantly for the very same purpose would have been obvious to one of ordinary skill in the art (See *In re Kerkhoven* 205 USPQ 1069).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreeni Padmanabhan, PhD., can be reached on (571) 272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

San-ming Hui
Patent Examiner
Art Unit 1617